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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/520,130	03/07/2000	Robert Arathoon	P1099R2	1353

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/520,130	ARATHOON ET AL.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/1/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on Oct. 1, 2003 has been entered.

Claims 12-14, 16-18 and 34-46 were canceled. Claims 48-63 were added. Claim 47 was amended.

Claims 47-63 are pending and examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Withdrawn:

3. The rejection of claims 12-14, 16-18, and 34-47 under 35 U.S.C. 112, first paragraph, on the grounds that the specification is not enabling for the full scope of the claimed inventions is withdrawn in view of the amendment.

4. The rejection of claims 12-14, 16-18, 31, 33-45 and 47 under 35 U.S.C. 112, first paragraph, on the grounds that the applicant was not in possession of the claimed inventions at

the time of filing, because the disclosure of the specification fails to adequately describe the claimed genus of compounds is withdrawn in view of the amendment.

5. The rejection of claim 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

6. The rejection of claims 12-14, 16-18, 34-38 under 35 U.S.C. 103(a) as being unpatentable over Vaughan (Nature Biotechnology, 14: 309-314, 1996; cited in the IDS) in view of Bosslet (U.S. Patent 5,591,828; issued Jan. 7, 1997; effective filing date of 6/20/1990) and further in view of either Ridgway (Protein Engineering, 9: 617-621, 1996), or Carter (WO 96/27011; published September 1996; cited in the IDS) is withdrawn in view of the amendment.

7. Claims 59-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ridgway (Protein Engineering, 9: 617-621, 1996; cited in the IDS), Carter (U.S. Patent 5,807,706; issued September 15, 1998; effective filing date of March 1, 1995) or Carter (WO 96/27011; published September 1996; cited in the IDS), in view of Kostelney (Journal of Immunology, 148: 1547-1553, 1992; cited in the IDS), and further in view of Vaughan (supra).

Claims 59-63 are drawn to bispecific antibodies, where the light chain of each of the binding domains is a common variable light chain domain that has at least 98% sequence identity to a first and a second variable light chain domain of a first and a second antibody. The bispecific antibodies are also characterized in that they comprise multimerization domains. Thus,

claims 59-63 reads on bispecific antibodies where each of the binding domains comprises the same light chain.

Any of Ridgeway, Carter (U.S.) or Carter (WO) teach methods for engineering multimerization domains of claims 59-63 comprising antibody CH3 regions onto polypeptides comprising heavy and light chain variable domains of antibodies for the purpose of making bispecific antibodies (see abstract, page 620, col. 2, fourth full paragraph of Ridgway; abstract of Carter (U.S.); page 6-7 of Carter (WO)). The Knobs and Holes multimerization domain of Ridgway , Carter (U.S.) or Carter (WO) forms an interface in which the interaction is between a cavity of one multimerization domain and a protuberance of a second multimerization domain, and further comprising a non-natuarally occurring disulfide bond between the two chains as recited in claims 61 and 62. Any of these reference teaches that the use of multimerization domains increases the efficiency of producing correctly paired bispecific antibodies.

Ridgeway, Carter (U.S.) or Carter (WO) fail to teach methods of making bispecific or multispecific antibodies where each of the separate antigen binding domains shares a common light chain.

Kostelney also teaches a method for making bispecific antibodies, and teaches a method for improving heterdimerization . Kosteney teaches a method that employs leucine zipper domains for the purpose of increasing yield of correctly paired bispecific antibodies. Additionally, Kostelney teaches that unwanted proteins may still be formed because of matching of different L chains and H chains (see page 1552, 1st col). Therefore, it appears that the prior art appreciated that there were two problems associated with methods for making bispecific antibodies. One problem was the formation of homodimers instead of heterodimers of heavy

chains. This problem is addressed by the inclusion of a multimerization domain, as taught by any of Ridgeway, Carter(U.S.) or Carter (WO) or Kostelney. The second problem is the problem of mismatched heavy and light chain pairings, taught by Kostelney.

Vaughan teaches an example of two scFvs where identical light chains are paired with two different heavy chains to bind to two different antigens, DTPA and CEA, and teaches methods for screening for scFvs with desired characteristics.

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have altered the methods of Ridgway, Carter (U.S.) or Carter (W.O) to include the step of finding a light chain that could be used for each of the binding domains and would pair with two different heavy chains to make two different antigen binding regions. One would have been motivated to use the method of Vaughn to look for such light chains because of the problem taught by Kostelney that even if antibodies are engineered to improve the heteroligomerization of two different heavy chains, unwanted antibody product may still be formed because of the mismatching of light chains with heavy chains.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 47-63 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30-51 of copending Application No. 09/863,693. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of application no. 09/863,693 are drawn to methods for making, and host cells comprising nucleic acids encoding, bispecific antibodies, where the method steps would produce bispecific antibodies that are within the scope of the claimed bispecific antibodies.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 47-63 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39-49 of copending Application No. 09/373,403. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of application no. 09/373,403 are drawn to multispecific antibodies that have the same or similar characteristics to the antibodies made by the claimed methods and host cells of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 47-63 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending Application No. 10/143,437. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of application no. 10/143,437 are drawn to methods of making multispecific antibodies where the multispecific antibodies have a common light chain. Such methods are within the scope of the instant methods are an obvious species.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Claims 47-58 are free of the prior art.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D. can be reached at (571) 272-0871.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (571) 272-1600.

Anne L. Holleran
Patent Examiner
March 22, 2004

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600